FEATURED CASE #19-04; ANSWERS
(Case study by Jim Perkins, © 2018)

Indian Immunohematology Initiative

1. What do you think might be going on here? Based on your hypothesis(ies) how might we proceed?

   The type-and-screen reveals the patient to be O negative with a positive antibody screen. All cells but one on the initial panel are reactive, at varying strengths, and the autocontrol and DAT are negative. An Rh phenotype, done per routine, showed the patient's most likely genotype to be rr.

   Given reactivity with most reagent cells varying strength at varying strength and a negative autocontrol/DAT we might initially consider the possibility of multiple alloantibodies or possibly method-dependent reactivity. Certain antibodies are ruled out, but the pattern of the positive reactions doesn't suggest any particular antibody specificity(ies).

   The technologist elected to run a second gel panel in the hope of finding additional "rule-out cell's", as well as running a panel by the LISS/tube method to rule out gel-dependent reactivity.

2. What is your impression now? What might you try next?

   The second gel panel is consistent with multiple alloantibodies, but it doesn't really help us as there are no more non-reactive cells. The LISS/tube panel rules out gel-dependent reactivity and shows that we are dealing with a "real antibody" or antibodies. Also there is a second non-reactive cell to use in ruling-out. Of the usual antibodies we are left with the possibilities of anti-E, anti-Fy^a, anti-Le^a, anti-M and anti-s, but none of these, and no combination of them, will explain all of the reactivity. So a less common answer must be considered.

   The technologist noted that the LISS/tube reactions were mostly weak and involved most donor RBCs. This suggested the possibility of an antibody showing the so-called "high-titer, low-avidity (HTLA)" phenomenon, so she decided to determine the antibody titer. Also, two to three hours had passed and the service was anxious to transfuse, so she elected to concurrently attempt to find crossmatch compatible RBCs using saline/tube technique with an increased serum:cell ratio, the crossmatch procedure then in use in the laboratory. Finally, reasoning that the latter technique might allow her to rule out additional antibodies, she elected to run additional RBCs with the crossmatches.

3. Now what do you think, and what would you do next?

   The titration shows that the patient's antibody has a high titer (16 but with microscopic reactions through a dilution of 1: 64) in spite of the relatively weak reactivity of the undiluted plasma, consistent with an antibody which typically shows the HTLA phenomenon. The results using the saline/tube technique with a serum/cell ration of 4:1 are somewhat anomalous in that the two screening cells tested were reactive as were the 4 donor cells, but the four selected panel cells are non-reactive, in spite of being tested by the same technologist. Nonetheless, to the extent that antibodies behaving as HTLA's can be regarded as clinically insignificant, the results are reassuring that none of the common, clinically-significant alloantibodies are detected.

   Although antibodies which display HTLA reactivity are generally regarded as benign, this is not entirely the case, and identifying their specificity is preferred. Testing with cells treated with ficin/papain and a sulfhydryl reducing agent can help determine the specificity of antibodies directed against high frequency antigens in general, including HTLA-type antibodies.

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4. What is your interpretation? How would you proceed?

   The most recent results demonstrate that the patient's antibody is directed against an antigen that is ficin sensitive and AET resistant. Inspection of a table of chemical effects on blood group antigens shows that this is consistent with anti-Chido/Rodgers (anti-Ch/Rg), which identify high frequency antigens carried on C4 molecules that bind to and coat RBCs. Anti-Ch/Rg typically behaves as HTLA. Since C4 is present in normal plasma, anti-Ch/Rg can be neutralized by pooled plasma. Note that the results with ficin treated RBCs cannot rule out antibodies directed against other ficin-sensitive antigens such as Duffy.

5. What is the interpretation? Are any clinical problems in recipients associated with this antibody? Do you see any problems with the workup as presented above?

   These results identify the antibody to be anti-Ch/Rg, although reference laboratories with access to rare cells might insist on running other CH/Rg negative RBCs for proof. Taken together the results rule out other blood group alloantibodies.

   Anti-Ch/Rg are not hemolytic. However, a few patients with anti-Ch/Rg have been reported to experience severe allergic reactions to plasma-containing components, and the author has seen one such case. This is one of the few situations in which we know the identity of the antigen mediating an allergic reaction. Presumably a patient with a history of such a reaction could be safely treated with washed RBCs.

   Regarding "problems with the workup" note that an autocontrol was only performed with the initial gel panel. It's probably acceptable that it was not performed with the less sensitive LISS/tube and saline/tube panels, but an autocontrol should have been done with the ficin and AET panels.

Take home points

The immunohematologic differential diagnosis for a patient plasma reacting with all or most cells on the initial panel(s).
The importance of ruling out method-dependent reactivity.
Approaches to identifying an antibody directed against a high frequency antigen, in particular the use of chemical inactivation of antigens.
The behavior of anti-Ch/Rg.